REMARKS

Claims 2, 3, and 5 are pending in this application. Claims 6, 8-10, and 22-29 are withdrawn from consideration. Claims 2, 3, 5, and 11-21 stand rejected. The Examiner has not proposed any rejections for Claims 7. Applicant respectfully submits that Claim 7 is patentable. However, for purposes of providing a complete response and to expedite prosecution of this case, Applicant submits that its arguments in relation to the rejections of Claim 2 also apply to Claim 7, in the event that Claim 7 is rejected on those grounds.

Applicant submits herewith the Declaration of Girish Shah under 37 C.F.R. §1.132 in support of this Amendment, a Request for Continued Examination, and an Information Disclosure Statement.

35 U.S.C. §112, First Paragraph Rejection

The Examiner maintains the rejection of claims 2, 3, and 5 under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the invention. Applicant respectfully traverses the rejection and requests withdrawal of the same.

The Examiner argues that the NEM peptide described in the specification shows no relation to the polypeptide of SEQ ID NO:6. Further, the Examiner mischaracterizes Applicant's description of the four derived cDNA sequences by stating that "the cDNA aside from that actually isolated (SEQ ID NO:2) is a derived sequence, not an actual isolation (see specification pg 8, 2nd & 3rd paragraph)."

As the Shah Declaration details, Applicant was in possession of an isolated cDNA and its expressed polypeptide prior to the filing of this application. The Applicant utilized this same

sample of isolated cDNA and expressed polypeptide to determine its useful characteristics. Initially, the isolated cDNA had been sequenced as SEQ ID NO:2 and the amino acid sequence of SEQ ID NO:1 was then deduced. The provisional application to which this application claims priority disclosed SEQ ID NO:1 as the NEM amino acid sequence. Subsequent to the provisional filing, however, Applicant re-sequenced the same sample of isolated cDNA and obtained the cDNA sequence of SEQ ID NO:3 and deduced the NEM amino acid sequence of SEQ ID NO:6, utilizing well-accepted methods in the art. In the present application, Applicant included four cDNA sequences it had derived from the same sample of isolated cDNA, including SEQ ID NO:3 and eight amino acid sequences, including SEQ ID NO.6, and noted that:

> Sequence IDs 2-5 . . . are alternative cDNA sequences derived from the NEM peptide [sic] based on Applicant's research and within reasonable margins for error. Peptide Sequence IDs 1, 6-8, 9-11, 12 are alternative sequences based on the cDNA Sequence IDs depending on the reading frame employed to translate same.

With this amendment, Applicant has amended this paragraph to read:

> SEQ ID NOs: 2-5 are alternative cDNA sequences derived from the isolated NEM cDNA based on Applicant's research and within reasonable margins for error. Peptide SEQ ID NOs: 1, 6-8, 9-11, 12 are alternative sequences based on the cDNA Sequence IDs depending on the reading frame employed to translate same.

One skilled in the art would recognize that the original application contained an error in that cDNA sequences are not derived from a peptide but from the cDNA itself. Therefore, Applicant explained in the specification that the same sample isolated cDNA was characterized by at least one of these four cDNA sequences and not necessarily SEQ ID NO:1. One skilled in the art would recognize that the properties of the novel polypeptide discussed in the application relate to at least one if not all of the polypeptides derived from the disclosed cDNA sequences, and then, could take each of these cDNA sequences and obtain the novel NEM polypeptide as recited in Claim 2, without undue experimentation.

35 U.S.C. §101 Rejection

The Examiner maintains the rejection of Claims 2, 3, and 5 under 35 U.S.C. §101 because the invention is allegedly directed to non-statutory subject matter. Previously in the Office Action, the Examiner withdrew this same rejection of Claim 2. Applicant assumes that the Examiner intended to maintain the §101 rejection of Claims 2, 3, and 5 because the claimed invention is allegedly not supported by either a credible, substantial and specific asserted utility, or a well-established utility. Applicant respectfully traverses the rejection and requests withdrawal of the same.

The Examiner argues that because the NEM protein of SEQ ID NO:1 shows no structural overlap or identity to that of SEQ ID NO:6, the utilities asserted for SEQ ID NO:1 cannot apply to SEQ ID NO:6. Further, the Examiner argues that because SEQ ID NO:6 is a derived sequence, there is no evidence that the biological effects and activities are similar to those of SEQ ID NO:1.

Both polypeptide sequences SEQ ID NOs: 1 and 6 were derived from cDNA sequences. Polypeptide SEQ ID NO:1 was deduced from cDNA SEQ ID NO:2 and polypeptide SEQ ID NO:6 was deduced from cDNA SEQ ID NO:3. Therefore, to ascertain a structural identity, one may look to the cDNA sequences from which the amino acid sequences were derived. As stated in the Declaration of Girish Shah, "[i]f the vector sequences were removed from SEQ ID NO:2 and compared to SEQ ID NO:3, the two sequences have a very high degree of homology." One skilled in the art would recognize that the differences in the cDNA sequences were due to vector inserts and sequencing errors. Therefore, once the vector portion of the sequence is removed, a skilled artisan would expect the polypeptides produced from these two cDNA to have similar characteristics and utility.

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The Examiner has acknowledged that utility has been established for a polypeptide having an amino acid sequence of SEQ ID NO:1. Applicant provided for reasonable error in characterizing the cDNA and amino acid sequences by including the following amended paragraph:

> SEQ ID NOs: 2-5 are alternative cDNA sequences derived from the isolated NEM cDNA based on Applicant's research and ***within reasonable margins for error***. Peptide SEQ ID NOs: 1, 6-8, 9-11, 12 are alternative sequences based on the cDNA Sequence IDs depending on the reading frame employed to translate same. (emphasis added)

With this paragraph, Applicant provides that even if SEQ ID NO:1 is not the accurate amino acid sequence then at least one of SEQ ID NOs: 6-8, 9-11, or 12 is. Regardless of whether the Examiner agrees that SEQ ID NO:1 and SEQ ID NO:6 have structural overlap or identity, Applicant has demonstrated in the specification, the Declaration of Girish Shah and in response to the §112, first paragraph rejection that the asserted utility of a NEM polypeptide expressed from the isolated cDNA is associated with at least one polypeptide characterized by the amino acid sequences disclosed in its application. A skilled artisan could take the disclosure from this application (the four cDNA sequences, SEQ ID NOs:2-5 and the eight polypeptides of the amino acid SEQ ID NOs: 1, 6-8,9-11, and 12) and determine which polypeptide possessed these utilities without undue experimentation.

35 U.S.C. §112, First Paragraph

The Examiner maintains the rejection of 2, 3, and 5 under 35 U.S.C. §112, first paragraph for not being supported by either a substantial or specific utility or a well established utility wherein one skilled in the art would not know how to use the claimed invention. Applicant respectfully traverses the rejection and requests withdrawal of the same.

Applicant respectfully submits that this rejection has been overcome in light of its response to the Examiner's 35 U.S.C. §101 rejection.

The Examiner has not presented separate rejections for independent Claim 7 nor dependent Claims 11-21. Applicant respectfully submits that in view of the arguments relating to Claims 2, 3, and 5, Claims 7 and 11-21 are likewise patentable.

CONCLUSION

Applicant submits that the claims are now in a condition for allowance, and requests early notification to that effect. Should the Examiner have any questions, please call the undersigned.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The paragraph beginning on page 7, line 22, has been amended as follows:

--Amino acid [Sequence No. 1] SEQ ID NO: 6 was prepared by first subcloning the complementary DNA [Sequence No. 2] SEQ ID NO: 3 in pRC vector (Invitrogen, San Diego, CA). The vector contains cytomegalovirus promoter upstream of the cloning site, and ensures high level expression of the cloned cDNA. The pRC plasmid containing NEM cDNA is then transfected in prostate cancer cell line PC-3M cells using Lipofectamine (Life Technologies, Inc., Gaithersburg, MD). In brief, PC-3M cells were plated at a density of 15,000 cells per well in a six-well culture plate and transfected 24 hours later with either the vehicle plasmid or the plasmids carrying cDNAs. Aliquots containing 2 mg plasmid and 4 mg Lipofectamine in 1 ml serum-free, protein-free Dulbecco's Modified Eagle's medium (DMEM) were incubated for 45 minutes and added to culture wells. The transfection media was replaced with the complete medium 16 hours later. Two days later, the cells were cultured in selection medium (complete medium containing 400 mg/ml of G418). Individual colonies of the transfectants (NEM PC-3M) were selected after four weeks of culture, dispersed with trypsin/EDTA and propagated further into fresh flasks. The conditioned media was collected, the cells are lysed with a cocktail of detergents and the expressed protein in both these fractions was obtained by affinity chromatography using ProBond^{TM} resin (as described by manufacturer's protocol, Invitrogen).--

The paragraph beginning on page 8, line 8, has been amended as follows:

-- [Sequence IDs 2-5 (Sequence Listings and Figs. 16-18)] SEQ ID NOs: 2-5 are alternative cDNA sequences derived from the isolated NEM cDNA [peptide] based on Applicant's research and within reasonable margins for error. Peptide [Sequence IDs 1, 6-8, 9-11, 12] SEQ ID NOs: 1, 6-8, 9-11, 12 are alternative sequences based on the cDNA Sequence IDs depending on the reading frame employed to translate same.--

The paragraph beginning on page 12, line 8, has been amended as follows:

--NEM mRNA was detected in prostate cancer specimens as well as cell lines using RT-PCR technique according to published procedures. The primers used in this procedure were: agaacctgtgtgctggcta (forward) and catatactaccccggcta (reverse). The total RNA from the specimens was extracted using a Quiagen RNA extraction kit (Quiagen, CA) according to the manufacturer's protocols, reverse transcribed using reverse transcriptase and amplified using the previously described primers pair. The reaction mixture was then separated on 1% agarose gel, and the amplicon of approximate size of 350 bp was detected as predicted according to [Sequence No. 1] SEQ ID NO: 6 in prostrate cancer specimens and DU-145, MCF-7 and PC-3M cancer cell lines. NEM mRNA was also detected by RT-PCR in certain breast cancer tissues demonstrating that NEM may be a marker for other cancers also, particularly the ones that show a high degree of differentiation into the neuroendocrine-type cells like small lung carcinoma, certain pancreatic cancers, renal cancer, adrenomedullary carcinoma etc.--

The heading on page 22, line 15, has been amended as follows:

--Detection of [Sequence 2] SEQ ID NO: 3--

The paragraph beginning on page 22, line 18, has been amended as follows:

--1. Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) by synthesizing NEM cDNA-specific amplifiers [(from Sequence ID 2)] SEQ ID NO: 3 in order to detect the expression of NEM mRNA by RT-PCR.--